REMARKS

Claims 39, 41 – 49 and 51 are currently pending. Claim 40 and 50 has been cancelled herein. No new matter has been added.

I. OBJECTIONS

The Examiner objected to the disclosure as informal because it contains missing text on page 1, line 5. The specification has been amended herein to recite the serial number "60/201,388." Thus, this objection should be withdrawn.

The Examiner also objected to pages 6-15 of the specification under 37 CFR 1.52(b) for having an inadequate top margin. Applicants amended the specification herein to include replacement pages 6-15, which contain the proper margins. Thus, this objection should be withdrawn.

Finally, the Examiner objected to a reference to "NOV12" when the Applicants intended to refer to "NOV11." Applicants ammended the specification herein to recite "NOV11." Thus, this objection should be withdrawn.

II. REJECTIONS UNDER 35 U.S.C.§ 101

Claims 39 to 51 are rejected under 35 U.S.C.§101, as the Examiner contends that the claimed invention has no apparent or disclosed specific and substantial credible utility. Applicants note that claims 40 and 50 have been cancelled herein. Thus, this rejection is moot with respect to these claims. Applicants respectfully disagree that claims 39, 41-49 and 51 are not supported by a specific and substantial credible utility. There are numerous locations in the specification in which utility of the claimed invention is established. For example:

> "The invention, in part is directed to methods of identifying a NOVX polypeptide or nucleic acid in a sample by contacting the sample with a compound that specifically binds to the polyptpeide or nucleic acid, and detecting complex formation, if present." (Page 3, lines 12-14)
>
> "The invention is provides methods of determining the presence of or predisposition of a NOVX-associated disorder in a subject by measuring the amount of NOVX in a sample." (Page 4, lines 3-10)

"Based on the bioactivity described in the medical literature for related molecules, a NOV11 nucleic acid or it encoded polypeptide may play a role in one or more aspects of tumor cell biology that alter the interactions of tumor epithelial cells with stromal components." (Page 78, lines 16-18)

"Predicted disease indications from expression profiling include a subset of human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas." (Page 78, lines 25-27)

"Probes based on the human NOVX nucleotide sequence can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. In various embodiments, the probe further comprises a label group attached thereto, *e.g.*, the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissue which misexpress a NOVX protein, such as by measuring a level of a NOVX-encoding nucleic acid in a sample of cells from a subject *e.g.*, detecting NOVX mRNA levels or determining whether a genomic NOVX gene has been mutated or deleted." (Page 91 lines 1-8)

"The nucleic acid molecules, proteins, protein homologues, and antibodies described herein can be used in one or more of the following methods: (a) screening assays; (b) detection assays (*e.g.*, chromosomal mapping, cell and tissue typing, forensic biology), (c) predictive medicine (*e.g.*, diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenomics); and (d) methods of treatment (*e.g.*, therapeutic and prophylactic)." (Page 124 lines, 24-27)

"Accordingly, one aspect of the present invention relates to diagnostic assays for determining NOVX protein and/or nucleic acid expression as well as NOVX activity, in the context of a biological sample (*e.g.*, blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant NOVX expression or activity." (Page 132, 11-18)

"Polynucleotides or oligonucleotides corresponding to any one portion of the NOVX nucleic acids of SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, and 45 may be used to detect DNA containing a corresponding NOV gene, or detect the expression of a corresponding NOVX gene, or NOVX-like

gene. For example, a NOVX nucleic acid expressed in a particular cell or tissue, as noted in Table 1, can be used to identify the presence of that particular cell type.

An exemplary method for detecting the presence or absence of NOVX in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting NOVX protein or nucleic acid (*e.g.*, mRNA, genomic DNA) that encodes NOVX protein such that the presence of NOVX is detected in the biological sample." (Page 135, line 15-25)

Specifically, as noted in the specification, a "subset of human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas" (Page 78, lines 25-27) can be distinguished from normal counterparts as demonstrated in the quantitative tissue expression analysis of Example 2. *See* Table 4 at Page 173, showing increased relative expression of nucleic acids encoding NOV11 in, for example, CNS carcinoma SW1783, SF-539, SNB-75, SNB-19, U251, Renal Carcimoa 786-0, RXF-393, lung carcinomas HOP-62, NCI-H522, NCI-H596, breast carcinoma T47D, BT-549, Ovarian carcinoma OVCAR-5, and melanoma Hs688(A). Therefore, expression of NOV11 nucleic acid is associated with certain types of cancer and, thereby, can be used to identify cancerous cells or tissue compared to normal tissues using the methods disclosed in the specification. Thus, contrary to the Examiner's assertion, Applicants contend that the claimed invention is supported by a specfic and substantial credible utility. Therefore, Applicant respectfully requests that this rejection be withdrawn.

II. REJECTIONS UNDER 35 U.S.C. § 112

Claims 39-51 are also rejected under 35 U.S.C. §112, first paragraph. The Examiner states that, since the claimed invention is not supported by either a specific and substantial credible utility or a well established utility, one skilled in the art would not know how to use the claimed invention. As noted above, Applicants submit that there is a specific and substantial credible utility for the claimed invention. Therefore, Applicants request this rejection be withdrawn.

Claims 40 and 50 are rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in a manner that reasonably conveys to one

skilled in the art that the inventor had possession of the claimed invention. While Applicants disagree with the Examiner, in order to expedite prosecution of the application, these claims have been cancelled. Therefore this rejection is moot.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

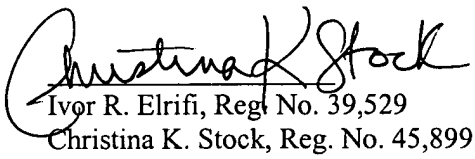

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TABLE 1: SUMMARY OF THE NOVX NUCLEIC ACIDS AND THEIR ENCODED POLYPEPTIDES

NOVX Number	Clone Identification Number	Total Length (bp)	Tissues in which expression is detected	ORF (aa)	ATG (nt #)	Stop Codon (nt #)	Protein Similarity	Cellular Localization	Signal Peptide Cleavage
NOV1	889240	836	5RH.43.4, 5PH.32, 5PH.29, 5RH.43.6, NQH1	169	189	696	Identities = 85/147 (57%), Positives = 107/147 (72%) with ACC:Q13445 PUTATIVE T1/ST2 RECEPTOR BINDING PROTEIN PRECURSOR - HOMO SAPIENS (HUMAN), 227 aa. Identities = 154/158 (97%), Positives = 155/158 (98%), with a 229 residue HUMAN CGI-100 PROTEIN identified by comparative gene cloning using *Caenorhabditis elegans* proteome as template (SPTREMBL-ACC: Q9Y3A6)	Outside (Cert=0.8200). Seems to have a cleavable N-term signal seq.	Most likely cleavage site between pos. 27 and 28: AAG-FT
NOV2	2855519	2342	fetal brain, placenta, thyroid gland, pancreas, uterus, fetal lung, psteosarcoma, pool of adrenal, mammary, prostate, testis, uterus, bone marrow*, melanoma*, pituitary*, thyroid*, spleen (*from mRNA rather than from total RNA)	547	110	1751	Identities = 188/342 (54%), Positives = 265/342 (77%) with ACC:O60301 KIAA0554 PROTEIN - HOMO SAPIENS (HUMAN), 674 aa (fragment); Identities = 300/544 (55%), Positives = 401/544 (73%) with ACC:O15184 CDC42-INTERACTING PROTEIN 4 - HOMO SAPIENS (HUMAN), 545 aa. 60% Identity and 74% similarity over 246	Nucleus (Cert=0.7000). Seems to have no N-terminal signal seq.	

							residues to 265 residue human SRC HOMOLOGY 3 DOMAIN (SH#)-CONTAINING PROTEIN 1 and 50% Identity and 67% Similarity over 168 residues to the 175 residue human SH3-CONTAINING PROTEIN 2.		
NOV3	2938100	711	5PH.28, 5PH.44.1, 5PH.48.2, 5PH.15, 5PH.48.3, 5PH.33, 5PH.19	115	143	488	Identities = 41/97 (42%), Positives = 47/97 (48%) with ACC:Q14210 E48 ANTIGEN PRECURSOR - HOMO SAPIENS (HUMAN), 128 aa. Identities = 111/116 (95%), Positives - 112/116 (96%) with 117 residue human secreted protein encoded by gene 89.	Plasma membrane (Cert=0.9190). Seems to have a cleavable N-term signal seq.	Most likely cleavage site between pos. 19 and 20: AQA-LD.
NOV4	3189601	1987	5PH.28, NQH1, NQH3, 5PH.19.6, 5PH.19.5, 5PH.44.3, 5RH.44.3, 5PH.44.5, 5PH.50.2 (thalamus)	152	991	1447	Identities = 90/100 (90%), Positives = 93/100 (93) with 102 residue EST from HUMAN BREAST TUMOUR-ASSOCIATED PROTEIN 47.	Microbody (peroxisome) (Cert=0.6400). Seems to have no N-terminal signal seq.	Most likely cleavage site between pos. 54 and 55: VXG-AA.
NOV5	3211101.1	1425	Pancreas, thyroid, peripheral blood, lymph node, bone, breast, ovary, kidney, lung, heart, parathyroid, brain, bone marrow, tonsils, adrenal gland, liver	252	587	1343	Identities = 75/224 (33%), Positives = 124/224 (55%) withACC:P05307 PROTEIN DISULFIDE ISOMERASE PRECURSOR (PDI) (EC 5.3.4.1) (PROLYL 4- HYDROXYLASE BETA SUBUNIT) (CELLULAR THYROID HORMONE BINDING	Plasma membrane (Cert=0.4600). Seems to have a cleavable N-term signal seq.	Most likely cleavage site between pos. 25 and 26: VAA-EV

							PROTEIN) (P55) - BOS TAURUS (BOVINE), 510 aa; Identities = 73/224 (32%), Positives = 121/224 (54%) with ACC:P07237 HUMAN PROTEIN DISULFIDE ISOMERASE PRECURSOR (PDI) (EC5.3.4.1)		
NOV21	3211101.0.120	1918	Pancreas, thyroid, peripheral blood, lymph node, bone, breast, ovary, kidney, lung, heart, parathyroid, brain, bone marrow, tonsils, adrenal gland, liver	252	1082	1838	Identities = 75/224 (33%), Positives = 124/224 (55%) withACC:P05307 PROTEIN DISULFIDE ISOMERASE PRECURSOR (PDI) (EC 5.3.4.1) (PROLYL 4- HYDROXYLASE BETA SUBUNIT) (CELLULAR THYROID HORMONE BINDING PROTEIN) (P55) - BOS TAURUS (BOVINE), 510 aa.	Plasma membrane (Cert=0.4600). Seems to have a cleavable N-term signal seq.	Most likely cleavage site between pos. 25 and 26: VAA-EV
NOV22	3211101.0.94	1914	Pancreas, thyroid, peripheral blood, lymph node, bone, breast, ovary, kidney, lung, heart, parathyroid, brain, bone marrow, tonsils, adrenal gland, liver	252	1078	1834	125/224 (55%) homology to BOS TAURUS PROTEIN DISULFIDE ISOMERASE PRECURSOR (PDI) (EC5.3.4.1) (PROLYL 4- HYDROXYLASE BETA SUBUNIT) (CELLULAR THYROID HORMONE BINDING PROTEIN) (P55) (ACC:P05307). 395///694 (56%) identity/homology to HOMO SAPIEN DISULFIDE ISOMERASE PRECURSOR (PDIp) mRNA (GENBANK-ID:HSU19948|acc:U19	Plasma membrane (Cert=0.4600). Seems to have a cleavable N-term signal seq.	Most likely cleavage site between pos. 25 and 26: VAA-EV

							948)		
NOV6	3218715	1481	--------	393	183	1362	Identities = 70/177 (39%), Positives = 107/177 (60%) with ACC:O04623 CODED FOR BY A. THALIANA CDNA T22670 - ARABIDOPSIS THALIANA (MOUSE-EAR CRESS), 968 aa. 100% identical to complete human protein encoded by the extended cDNA sequences represented in X97813-X97906.	Outside (Cert=0.3700). Seems to have a cleavable N-term signal seq.	Most likely cleavage site between pos. 22 and 23: TLS-KS
NOV7	3247716	811	5RH.25, 5PH.48.5, 5PH.48.2, 5PH.31, 5PH.33, 5RH.35, 5PH.48.6, 5PH.28	132	91	487	Identities = 14/30 (46%), Positives = 18/30 (60%) with ACC:Q15309 RHODOPSIN - HOMO SAPIENS (HUMAN), 51 aa (fragment).	Plasma membrane (Cert=0.7000). Seems to have a cleavable N-terminal signal seq.	Most likely cleavage site between pos. 57 and 58: IVA-NI
NOV8	3467082	734	--------	105	146	461	Identities = 11/19 (57%), Positives = 15/19 (78%) with ACC:E158503 INTERFERON ALPHA-L PSEUDOGENE, 5' END PRECURSOR - HOMO SAPIENS (HUMAN), 30 aa (fragment).	Plasma membrane (Cert=0.4600). Low probability of having a cleavable N-terminal signal sequence.	
NOV9	3540000	1659	5RH.19. 5PH.30, 5PH.31, 5RH.22, 5PH.19.3, 5PH.44.1, 5PH.11, 5PH.29, 5PH.44.4, 5PH.44.5, 5PH.24, 5RH.43.2, 5PH.48.5, fetal lung	410	244	1474	27% Identities / 47% Positives with ACC:O14915 IL-1 RECEPTOR ACCESSORY PROTEIN - HOMO SAPIENS (HUMAN), 570 aa. 100% identical to an IL-1 analog SIGAR protein having anti-inflammatory and anti-autoimmune disease activity.	Golgi body (Cert=0.9000). Seems not to have a cleavable N-terminal signal seq.	

NOV10	10360189	3361	thymus gland, spleen, brain/pituitary gland, liver/fetal liver, kidney/fetal kidney, bone/osteosarcoma, heart, adrenal gland	732	813	3009	Identities = 257/701 (36%), Positives = 360/701 (51%) with ACC:Q17429 HYPOTHETICAL 96.8 KD PROTEIN B0024.14 IN CHROMOSOME V - CAENORHABDITIS ELEGANS, 884 aa; Identities = 142/529 (26%), Positives = 215/529 (40%) with ACC:BAA11680 NEL-RELATED PROTEIN - HOMO SAPIENS Identities = 715/721 (99%), Positives = 716/721 (99%) with the 1036 residue HUMAN SECRETED PROTEIN CLONE dj167_19.	Nucleus (Cert=0.3000). Seems not to have a cleavable N-terminal signal seq.	
NOV11	10129612.0.19	1431	Heart	381	69	1212	Identities = 74/134 (55%), Positives = 96/134 (71%) with ACC:O14667 GAMMA-HEREGULIN - HOMO SAPIENS (HUMAN), 768 aa.	Endoplasmic reticulum (membrane) (Cert=0.8500). Seems not to have a cleavable N-terminal signal seq.	
NOV12	10219646.0.58	2116	brain, brain/pituitary gland	404	517	1729	Identities = 200/374 (53%), Positives = 269/374 (71%) with TREMBLNEW-ACC:AAD17540 CELL ADHESION MOLECULE - HOMO SAPIENS (HUMAN), 433 aa. Identities = 327/329 (99%), Positives = 327/329 (99%) with 444 residue HUMAN BETA-SECRETASE.	Plasma membrane (Cert=0.4600). Seems to have a cleavable N-term signal seq.	Most likely cleavage site between pos. 24 and 25: AAS-KN
NOV13	17954491.0.160	2862	spleen, brain/thalamus, breast/mammary gland, adrenal gland	683	508	2557	Identities = 227/541 (41%), Positives = 335/541 (61%) with	Plasma membrane (Cert=0.6000). Seems not to have a cleavable	

							ACC:BAA34488 KIAA0768 PROTEIN - HOMO SAPIENS (HUMAN), 872 aa (fragment). Identities = 680/683 (99%), Positives = 682/683 (99%) with 690 residue HUMAN PROTEIN PRO228.	N-terminal signal seq.	
NOV14	17954491.0.61	2760	spleen, brain/thalamus, breast/mammary gland, arenal gland	645	520	2455	Identities = 227/541 (41%), Positives = 335/541 (61%) with ACC:BAA34488 KIAA0768 PROTEIN - HOMO SAPIENS (HUMAN), 872 aa (fragment). Identities = 643/645 (99%), positives = 644/645 (99%) with 690 residue HUMAN PROTEIN PRO228.	Plasma membrane (Cert=0.6000). Seems not to have a cleavable N-terminal signal seq.	
NOV23	17954491.0.223	3801	spleen, brain/thalamus, breast/mammary gland, adrenal gland	645	460	2395	Identities = 227/541 (41%), Positives = 335/541 (61%) with ACC:BAA34488 KIAA0768 PROTEIN - HOMO SAPIENS (HUMAN), 872 aa (fragment). Identities = 643/645 (99%), positives = 644/645 (99%) with 690 residue HUMAN PROTEIN PRO228.	Plasma membrane (Cert=0.6000). Seems not to have a cleavable N-terminal signal seq.	
NOV15	20613648.0.12	727	pancreas, salivary gland, pituitary gland	83	312	560	Identities = 15/46 (32%), Positives = 25/46 (54%) with ACC:O81115 RECEPTOR-LIKE KINASE - TRITICUM AESTIVUM (WHEAT), 284 aa (fragment), Identities = 10/36 (27%), Positives =	Mitochondrial matrix space (Cert=0.59). Moderate probability that there is an N-terminal signal seq.	Most likely cleavage site between pos. 25 and 26: CRT-DL

							17/36 (47%) with ACC:P04155 PS2 PROTEIN PRECURSOR (HP1.A) (BREAST CANCER ESTROGEN-INDUCIBLE PROTEIN), 84 aa.		
NOV16	3541612.0.13	2741	bone/osteosarcoma, thymus gland, fetal kidney, bone marrow, lymph node	578	288	2022	Identities = 37/43 (86%), Positives = 39/43 (90%) with ACC:Q04842 EPIDERMAL GROWTH FACTOR RECEPTOR-RELATED PROTEIN - HOMO SAPIENS (HUMAN), 80 aa (fragment).	Nucleus (Cert=0.8920). Seems not to have a cleavable N-terminal signal seq.	
NOV17	3541612.0.88	2596	bone/osteosarcoma, thymus gland, fetal kidney, bone marrow, lymph node	708	289	2413	Identities = 70/80 (87%), Positives = 75/80 (93%) with ACC:Q04842 EPIDERMAL GROWTH FACTOR RECEPTOR-RELATED PROTEIN - HOMO SAPIENS(HUMAN), 80 aa (fragment).	plasma membrane (Cert=0.6000). Seems not to have a cleavable N-terminal signal seq.	
NOV18	3726392	705	5RH.43.4, 5PH.14, 5PH.44.7, 5RH.25, 5PH.19.3	137	135	546	Identities = 19/51 (37%), Positives = 21/51 (41%) with ACC:P71959 HYPOTHETICAL 9.9 KD PROTEIN CY441.31 – MYCOBACTERIUM TUBERCULOSIS, 90 aa; Identities = 25/73 (34%), Positives = 36/73 (49%) with ACC:P24347 STROMELYSIN-3 PRECURSOR (EC 3.4.24.-) (MATRIX MET	plasma membrane (Cert=0.650). Seems to have a cleavable N-terminal signal seq.	Most likely cleavage site between pos. 52 and 53: APS-ED.
NOV19	428773-1	1150	5PH.50.2 (thalamus), 5RH.26,	156	389	857	Identities = 40/112	plasma membrane	Most likely cleavage site

			NQH1				(35%), Positives = 61/112 (54%) with ACC:Q04941 INTESTINAL MEMBRANE A4 PROTEIN (DIFFERENTIATION-DEPENDENT PROTEIN A4) - HOMO SAPIENS (HUMAN), 152 aa. 100% identical to over 156 residues of HUMAN MEMBRANE SPANNING PROTEIN MSP-4.	(Cert=0.60000. Seems to have a cleavable N-terminal signal seq.	between pos. 58 and 59: ISA-YM.
NOV20	4321501.0.65	1611	placenta, lymph node	260	505	1285	Identities = 73/204 (35%), Positives = 119/204 (58%) with ACC:Q19985 F40E10.6 PROTEIN - CAENORHABDITIS ELEGANS, 595 aa	plasma membrane (Cert=0.4600). Seems to have a cleavable N-term signal seq.	Most likely cleavage site between pos. 29 and 30: VVA-VP

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